WHAT IS CLAIMED IS:

1. A method for producing mammalian proteins comprising:

growing mammalian secondary expression host cells comprising multiple copies of an amplifable region comprising a target gene heterologous to said secondary expression host and expressing a protein of interest and an amplifiable gene, whereby said target gene is expressed and said protein is produced;

wherein said secondary host expression cells are produced by the method comprising:

transforming primary mammalian cells comprising said target gene with a construct comprising an amplifiable gene and at least one flanking region of a total of at least about 150 bp homologous with a DNA sequence at the locus of the coding region of said target gene to provide amplification of said target gene, wherein said amplifiable gene is at a site which does not interfere with the expression of said target gene, whereby said construct becomes homologously integrated into the genome of said primary cells to define an amplifiable region;

selecting for primary cells comprising said construct by means of said amplifiable gene or other marker present in said construct;

isolating DNA portions of said genome from said primary cells, wherein said portions are large enough to include all of said amplifiable region;

transforming secondary expression host cells with said primary cell DNA portions and cloning said transformed secondary expression host cells to produce clones of said secondary expression host cells differing in said DNA portions present in said secondary expression host cells;

selecting clones of said mammalian secondary expression host cells comprising said amplifiable

region; and

amplifying said amplifiable region by means of an amplifying agent, wherein said amplifying is prior to said isolating or after said selecting and prior to said growing.

2. A method according to Claim 1, wherein said amplifiable gene is a mammalian DHFR gene.

3. A method according to Claim 1, wherein said portions are metaphase chromosomes.

4. A method according to Claim 1, wherein said portions are restriction fragments.

5. A method according to Claim 1, wherein said primary cells are human cells.

6. A method according to Claim 5, wherein said human cells are fibroblast cells.

7. A method according to Claim 1, wherein said construct comprises a biocidal marker providing resistance to a biocide for said primary host cells.

8. A method for producing mammalian proteins comprising:

transforming mammalian primary mammalian cells comprising said target gene with a construct comprising an amplifiable gene and at least one flanking region of at least about 150 bp homologous with a DNA sequence within 50 kb of the coding region of said target gene, wherein said amplifiable gene is at a site which does not interfere with the expression of said target gene, whereby said construct becomes homologously integrated into the genome of said primary cells to define an amplifiable region comprising said amplifiable gene and

said target gene in said genome;

selecting for primary cells comprising said construct by means of said amplifiable gene or other marker present in said construct;

isolating DNA portions of said genome from said primary cells, wherein said portions are large enough to include all of said amplifiable region;

transforming mammalian secondary expression host cells with said primary cell DNA portions, wherein said secondary expression host cells are of a different species from said primary host cells, and cloning said transformed secondary expression host cells to produce clones of said secondary expression host cells differing in said DNA portions present in said secondary expression host cells;

selecting clones of said mammalian secondary expression host cells comprising said amplifiable region;

amplifying said amplifiable region by means of an amplifying agent, wherein said amplifying is prior to said isolating or after said selecting; and

growing said secondary expression host cells comprising multiple copies of said amplifiable region, whereby said target gene is expressed and said protein is produced.

9. A method according to Claim 8, wherein said amplifying is with said secondary expression host cells.

10. A method according to Claim 8, wherein said primary cells are human cells.

11. A method according to Claim 10, wherein said human cells are diploid fibroblast cells.

12. A method according to Claim 8, wherein said

amplifiable gene is a mutated DHFR gene having a higher Km than the wild-type gene.

13. A method according to Claim 12, wherein said secondary host expression cell is DHFR deficient.

14. A method according to Claim 8, wherein said construct further comprises a marker gene separated from said amplifiable region by an homologous flanking region.

15. A human cell comprising an amplifiable gene at other than its wild-type site in the human genome and within the locus of a target gene expressing a protein to provide amplification of said target gene.

16. A human cell according to Claim 14, wherein said cell is a normal cell.

17. A human cell according to Claim 14, wherein said cell is a neoplastic cell.

18. A human cell according to Claim 14, wherein said amplifiable gene is a DHFR gene.

19. A mammalian cell other than a human cell for expression of mammalian proteins in culture comprising an amplifiable region comprising an amplifiable gene within 10kb of a human wild-type gene expressing a protein, wherein said two genes are separated by substantially solely human wild-type sequence associated with said target gene and the flanking sequence associated with the amplifiable gene.

20. A method for producing cells for expression of a heterologous protein in culture, said method comprising:

transforming mammalian primary cells comprising said target gene with a construct comprising an amplifiable gene and at least one flanking region of at least about 150bp homologous with a DNA sequence within 10kb of the coding region of said target gene, wherein said amplifiable gene is at a site which does not interfere with the expression of said target gene, whereby said construct becomes homologously integrated into the genome of said primary cells to define an amplifiable region comprising said amplifiable gene and said target gene in said genome;

selecting for primary cells comprising said construct by means of said amplifiable gene or other marker present in said construct;

isolating DNA portions of said genome from said primary cells, wherein said portions are large enough to include all of said amplifiable region;

transforming mammalian secondary expression host cells with said primary cell DNA portions, wherein said secondary expression host cells are of a different species from said primary host cells, and cloning said transformed secondary expression host cells to produce clones of said secondary expression host cells differing in said DNA portions present in said secondary expression host cells;

selecting clones of said mammalian secondary expression host cells comprising said amplifiable region; and

amplifying said amplifiable region by means of an amplifying agent, wherein said amplifying is either prior to said isolating or after said selecting.

21. A method according to Claim 20, wherein said amplifying is with said secondary expression host cells.

22. A method according to Claim 20, wherein

said primary cells are human cells.

23. A method according to Claim 22, wherein said human cells are diploid fibroblast cells.

24. A method according to Claim 20, wherein said amplifiable gene is a mutated DHFR gene having a higher Km than the wild-type gene.

25. A method according to Claim 24, wherein said secondary host expression cell is DHFR deficient.